

LIST OF TABLES

Table 1-1	Summary of Current U.S. Legislation for Using Acute Systemic Toxicity Data for Product Labeling	1-15
Table 1-2	Regulatory Classification Systems for Acute Oral Toxicity	1-16
Table 2-1	Vehicle Control OD ₅₄₀ Ranges	2-19
Table 2-2	Refeeding/No Refeeding Data	2-31
Table 2-3	Error Rates in Phase Ib by Laboratory and Test Method	2-36
Table 2-4	Cell Culture Seeding Densities	2-47
Table 2-5	Comparison of Concentrations Tested in Various Solubility Protocols	2-54
Table 3-1	UN GHS Classification Scheme for Acute Oral Toxicity.....	3-4
Table 3-2	Candidate Chemicals for the 3T3 and NHK Test Methods Validation Study	3-7
Table 3-3	Distribution of Candidate Chemicals and Reference Substances by Source and Toxicity Category.....	3-19
Table 3-4	Selected Chemicals: Distribution of Registry of Cytotoxicity (RC) Chemicals and RC Outliers by Toxicity Category.....	3-20
Table 3-5	Distribution of Chemical Class for the 72 Reference Substances by Toxicity Category	3-24
Table 3-6	Distribution of Product/Use Class for the 72 Reference Substances by Toxicity Category	3-26
Table 3-7	Reference Substances Metabolized to Active Metabolites	3-27
Table 3-8	Reference Substances Tested in Phases Ib and II.....	3-29
Table 4-1	Internet Accessible Databases with LD ₅₀ Information.....	4-4
Table 4-2	Reference LD ₅₀ Values by GHS Category	4-11
Table 4-3	GHS Toxicity Category Matches for the Initial and Reference LD ₅₀ Values	4-15
Table 4-4	Maximum:Minimum LD ₅₀ Ratios by GHS Toxicity Category	4-17
Table 5-1	Reference Substances Affected by Stopping Rule.....	5-9
Table 5-2	Positive Control (SLS) Data by Phase	5-11
Table 5-3	3T3 and NHK NRU Test Method Summary IC ₅₀ Data from the Laboratories .	5-20
Table 5-4	Comparison of 3T3 and NHK IC ₅₀ Geometric Means.....	5-32
Table 5-5	Difference in 3T3 and NHK IC ₅₀ Values as Orders of Magnitude.....	5-34
Table 5-6	Validation Study Timetable.....	5-38
Table 5-7	Solubility Results (data presented in mg/mL)	5-41
Table 5-8	Reference Substances with Precipitate (PPT) and Volatility Issues.....	5-46

Table 6-1	Linear Regression Analyses of the 3T3 and NHK NRU and <i>In Vivo</i> Rodent LD ₅₀ Test Results	6-6
Table 6-2	Linear Regression Analyses to Improve the Prediction of Rodent LD ₅₀ from <i>In Vitro</i> NRU IC ₅₀ Using the RC Regression	6-10
Table 6-3	Substances Deleted from the Evaluations of the 3T3 and NHK NRU Test Methods and Regressions Due to Mechanisms of Toxicity Not Expected to Be Active in the 3T3 and NHK Cell Cultures	6-16
Table 6-4	Prediction of GHS Toxicity Category by the 3T3 and NHK NRU Test Methods and the RC Millimole Regression	6-18
Table 6-5	Prediction of GHS Toxicity Category by the RC Rat-Only Weight Regression	6-23
Table 6-6	Prediction of GHS Toxicity Categories by RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity.....	6-27
Table 6-7	Comparison of Regressions and <i>In Vitro</i> NRU Test Methods for Performance in Predicting GHS Toxicity Categories.....	6-31
Table 6-8	Linear Regressions for Substances Tested in Phases Ib and II	6-37
Table 7-1	Reference Substances That Failed to Yield IC ₅₀ Values and Number of Reference Substances Available for Intralaboratory Reproducibility Analyses	7-5
Table 7-2	Number of Reference Substances Tested vs Number of Reference Substances Yielding IC ₅₀ Values in Each GHS Toxicity Category for Two Sets of LD ₅₀ Values	7-5
Table 7-3	Reproducibility Results for the 3T3 and NHK NRU Test Methods.....	7-7
Table 7-4	Reference Substances with Significant Differences between Laboratories for 3T3 NRU Test Method Results	7-15
Table 7-5	Reference Substances with Significant Differences between Laboratories for NHK NRU Test Method Results	7-16
Table 7-6	Summary of CV Results for the 3T3 and NHK NRU Test Methods.....	7-18
Table 7-7	Intralaboratory CV by Chemical Characteristics for the 3T3 and NHK NRU Test Methods	7-20
Table 7-8	Interlaboratory CV by Chemical Characteristics for the 3T3 and NHK NRU Test Methods	7-23
Table 7-9	ANOVA Results for SLS IC ₅₀ from the 3T3 NRU Test Method	7-31
Table 7-10	Linear Regression Analysis of SLS IC ₅₀ Over Time	7-32
Table 7-11	ANOVA Results for SLS IC ₅₀ from the NHK NRU Test Method.....	7-33
Table 7-12	Solvent Determinations by Laboratory	7-35
Table 8-1	SMT-Recommended Documentation for FAL Laboratory.....	8-4

Table 8-2	Error Rates.....	8-13
Table 8-3	Definitive Test and Positive Control (PC) Test Failure Rates.....	8-14
Table 8-4	Definitive Test and PC Test Success Rates for 3T3 and NHK NRU Test Methods (Combined Total Tests)	8-15
Table 8-5	Coefficients of Variation.....	8-15
Table 8-6	GHS Toxicity Category Predictions by Laboratory.....	8-16
Table 9-1	EU Classes of Acute Oral Toxicity.....	9-7
Table 9-2	Correct Predictions of <i>In Vivo</i> Phototoxicants by NHK NRU Phototoxicity Assay	9-20
Table 10-1	Change in Animal Use with Dose-Response Slope for the UDP	10-10
Table 10-2	Mean Animal Use for the UDP Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with Various Regressions	10-12
Table 10-3	Animal Use for the UDP by GHS Toxicity Category Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with the RC Millimole Regression	10-15
Table 10-4	Animal Use for the UDP by GHS Toxicity Category Using Starting Doses Based on the NRU Test Methods with the RC Rat-Only Weight Regression	10-17
Table 10-5	Animal Use for the UDP by GHS Toxicity Category Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with the RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity	10-20
Table 10-6	Animal Deaths for the UDP Using Starting Doses Based on the 3T3 and NHK NRU Test Methods	10-24
Table 10-7	Change in Animal Use with Dose-Response Slope for the ATC	10-28
Table 10-8	Animal Use for the ATC Using Starting Doses Based on NRU Test Methods with Various Regressions.....	10-30
Table 10-9	Animal Savings for the ATC by GHS Toxicity Category Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with the RC Millimole Regression	10-32
Table 10-10	Animal Savings for the ATC by GHS Toxicity Category Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with the RC Rat-Only Weight Regression	10-35
Table 10-11	Animal Savings for the ATC by GHS Toxicity Category Using Starting Doses Based on the 3T3 and NHK NRU Test Methods with the RC Rat-Only Weight Regression Excluding Substances with Specific Mechanisms of Toxicity	10-38
Table 10-12	Animal Deaths for the ATC Using Starting Doses Based on the 3T3 and NHK NRU Test Methods	10-41

Table 11-1	Costs for Cell Culture Materials and Commercial Laboratory <i>In Vitro</i> Cytotoxicity Testing.....	11-12
Table 11-2	Commercial Prices for Conducting <i>In Vivo</i> Acute Toxicity Testing.....	11-14